Table 12: **Pol**

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
Pol( )	RT( )		HIV-1 infection	human( )	[Buseyne (1998a)]
• This study showed a correlation between strong CTL memory and breadth of response in 7-12 month old infants, and remaining AIDS-free for the first year of life, higher absolute CD4 and CD8 cells, and lower viral load					
Pol( )	p66( )		HIV-1 infection	human( )	[Zheng (1999)]
• Protein delivery (gp160 LAV, p66 LAV, and p24 NY5) to human dendritic cells (DC) with liposomes provides enhanced memory CTL response relative to delivery of protein alone • Chloroquine administration enhanced epitope presentation, and brefeldin A and peptide aldehyde inhibitors inhibited antigen presentation, suggesting epitopes were processed by a classical proteasome pathway					
Pol( )	Pol( )		HIV-1 infection	human( )	[Wasik (2000)]
• HIV+ infants that progressed rapidly to AIDS had lower Th1 responses and decreased production of β-chemokines and IL-2 relative to other HIV+ infants • No HIV+ infants had no demonstrable CTL at birth, but Th1 responses accompanied by CTL responses developed in children with slowly progressive disease, and not in rapid progressors • CTLp frequencies were determined by limiting dilution using autologous B cells infected with vaccinia/HIV constructs					
Pol( )	Pol( )		Vaccine	human( )	[Salmon-Ceron (1999)]
Vaccine: *Vector/type:* canarypox *Strain:* LAI, MN *HIV component:* gp41, Gag, Pro, V3 • The vaccine used was a rec canarypox with HIV-1 gp120 MN, tm/gag/protease LAI (vCP205), alone or with p24E-V3 MN synthetic peptide (CLTB-36)) • Twenty HIV negative subjects were vaccinated in phase I trial with combinations of vCP205 and CLTB-36 • Immunization with vCP205 induced HIV-1-specific ABs to gp160, V3, and p24 antigens, and CTL immune responses against vCP205 were detected after the fourth immunization in 33% of the subjects against Env, Gag and Pol, but the CLTB-36 peptide did not produce AB or CTL immune responses against p24 or gp160					
Pol( )	Pol(172–219 clade B)		Vaccine	human( )	[Gorse (1999)]
Vaccine: *Vector/type:* canarypox prime with rgp120 boost *Strain:* LAI and SF2 *HIV component:* Env, Gag, Pro, Nef, Pro • The vaccine used was rec canarypox expressing HIV-1 env, gag, pol, nef and protease (vCP300) with or without administration of HIV-1 SF-2 rgp120 • In vitro inducible CTL activity against HIV-1 Env, Gag, Pol, and Nef antigens was observed in 79% (15/19) of vaccine recipients • The combination of vCP300 and vP1291 together resulted in an overall increase in CTL induction and detection sensitivity					

Pol( ) Pol( ) HIV-1 infection human( ) [Betts (1999)]
- This study demonstrated an inverse correlation between HIV Type I plasma viral load and CTL activity directed against HIV-1 Pol, and stronger combined effects of Pol- and Env-specific CTL, in long-term survivors (LTS) of HIV-1 infection

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Pol( ) Pol( ) HIV-1 infection human( ) [Aladdin (1999)]
- In vitro measurements of CTL-activity by Cr release assay in bulk culture showed no correlation between CTL-activity (gp120, Gag, Pol and Nef) and disease progression as measured by viral load, CD4 and time to death

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Pol( ) RT( ) HIV-1 infection human( ) [Buseyne (1998b)]
- In infants with positive CTL responses, most responses showed cross-clade reactivity with somewhat diminished recognition of epitopes from different subtypes

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Pol( ) RT( ) Vaccine murine( ) [Kim (1997b)]

Vaccine: *Vector/type:* DNA *HIV component:* Gag, Pol, Vif, Env *Stimulatory Agents:* B7, IL-12
- A gag/pol, vif or gp160 DNA vaccine, when delivered in conjunction with the plasmid encoding the co-stimulatory molecules B7 and IL-12, gave a dramatic increase in both the cytotoxic and proliferative responses in mice
- When IL-12 was present, CTL response could be detected even without *in vitro* stimulation

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Pol( ) RT( ) HIV-1 infection human( ) [Trickett (1998)]
- Twelve HIV-1 infected patients were re-infused with their own lymphocytes, cryopreserved from an earlier time point in the infection
- Improvement in CD4+ and CD8+ T-cells were seen in 7/12, and an increase in the CTL response to Pol was seen in one patient

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Pol( ) RT( ) HIV-1 infection human( ) [Froebel (1997)]
- Two HIV-1 infected children with contrasting disease courses were followed longitudinally – one died of AIDS, the other is a long-term non-progressor
- Reactivity against Gag, Pol, Env and Tat proteins was tested by PBMC bulk cultured cells reacting with protein expressed in vaccinia constructs in autologous EBV transformed B cells
- The child who progressed consistently had CTL against Pol and Tat
- The long-term non-progressing child had no detectable CTL, but was heterozygous for a mutation in the CCR5 receptor and for HLA-B49, which has been shown to be associated with slower progression

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Pol( ) Pol( ) HIV-1 infection human( ) [Betts (1997)]
- 6/8 individuals from Zambia infected with C clade virus had CTL that were able to make response to B clade HIV-1 IIIB vaccinia-expressed Gag, Pol and Env proteins
- A vigorous cross-clade response was not limited to a particular protein, and the level of recognition of different proteins varied among the six patients

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Pol( ) RT( ) HIV-1 infection human( ) [De Maria (1997)]
- CD3+ cells that also carry a natural killer cell receptor (NKR+) can exhibit down regulation of T-cell function

- Anti-NKR IgM MAb masked this inhibitory function and increased HIV-1 specific CTL activity in phytohemagglutinin-activated PBMC cultured in the presence of IL-2 from 3/5 patients, and in one other case anti-NKR MAb brought HIV-1 specific CTL activity to detectable levels

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Pol( ) Pol( ) HIV-1 exposed seronegative human( ) [Goh (1999)]

- 13/37 exposed uninfected individuals with repeated high-risk sexual exposure had HIV-1 specific CTL against Env, Gag, Pol, or a combination of proteins – CTL activity was correlated with a CCR5 wildtype genotype
- In this group, the highest CTLp frequencies were directed at Gag, but the most common response was to Env and four individuals had responses to multiple HIV-1 proteins

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Pol( ) Pol( ) Vaccine human( ) [Evans (1999)]

Vaccine: *Vector/type:* canarypox *HIV component:* gp120, gp41, Gag, Pro, Nef, RT

- A Canarypox vaccine expressing gp120, gp41, Gag, Protease, Nef and Pol CTL epitopes gave rise to CTL that could be detected in 61% of the volunteers – responses to Gag, Env, Nef and Pol were detected 3-6 months after the last vaccination

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Pol( ) Gag/Pol( ) Vaccine chimpanzee( ) [Kim (1998)]

Vaccine: *Vector/type:* DNA *HIV component:* Env, Gag, Pol *Stimulatory Agents:* CD86, CD80

- The study explores the use of co-stimulatory molecules co-expressed with an HIV-1 immunogen in a DNA vaccine to enhance the immune response – co-expression of CD86, but not CD80, dramatically increased both HIV Env and Gag/Pol specific CTL and Th proliferative responses

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Pol( ) Pol( ) HIV-1 infection human( ) [Jin (1998a)]

- CTL precursor frequencies were determined in HIV-1 infected pregnant women, and significantly higher CTLp frequencies to Pol and Nef were found in non-transmitting mothers than in transmitting mothers;

Pol( ) Pol( ) none HIV-1 infection human( ) [Young (2001)]

- Addition of recombinant human IL-12 (rhIL-12) to cultures increased HIV-specific lysis of HIV-Gag, Pol and gp120 vaccinia expressed antigens (11/15 tested increased lysis by > 5%) if the culture was derived from HIV+ individuals who had CD4 cells/μl > 500
- 2/10 individuals with <200 CD4 cells/μl, and 3/10 individuals with 200-500 CD4 cells/μl, had an increase of >5% upon treatment of the culture with rhIL-12, so a few individuals in late stage disease had CD8 cells that maintained responsiveness to rhIL-12

Pol( ) RT( ) HIV-1 infection human( ) [Cao (2000)]

- HIV-1 subtypes A and D dominate the Ugandan epidemic, and a vaccine trial using B clade antigen is underway – this study addresses relative levels of cross-reactive CTL responses in HIV infected Ugandans to A, D, and B clade recombinant vaccinia viruses expressing Gag, Env, Pol, RT or Nef from HIV-1 clades A, B, and D
- Proteins corresponding to the subtype of the infecting strains tended to trigger higher levels of CTL response measured by percent-specific lysis, but there was extensive inter-subtype cross-reactivity with B clade proteins and the co-circulating subtype

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Pol( ) Pol( ) HIV-1 infection human( ) [White (2001)]

- HIV-specific CTL activity was detected in the female reproductive tract of only 1/3 HIV-infected women who underwent a hysterectomy, although CTL could be identified in the PBMC of all three women

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Pol( )	Pol( )	HIV-1 infection	human( )	[Jin (2000a)]

- The CTL precursor level (CTLp) was measured in long term non-progressors (LTNP) with low viral load using limiting dilution analysis and measuring CTL against Env Gag and Pol expressed in vaccinia in autologous targets
- LTNPs have high memory CTL numbers and low viral load

Pol( )	Pol( )	HIV-1 exposed seronegative	human( )	[Rowland-Jones (2001)]

- This is a review that summarizes observations about HIV-specific CTL found in the HIV-1 exposed persistently seronegative (HEPS) population
- The CTL responses assayed by ELISPOT and by CTL precursor frequencies by limiting dilution analysis indicate that CTL in HEPS individuals tend to be of a lower magnitude than in chronic HIV-1 infections – the responses in HEPS cases are below the level of detection by tetramer assays
- CD8+ CTL responses tend to be detectable in HEPS subjects only if they are recently exposed, and the response diminishes if exposure is reduced – it is not clear if there is a stable memory population in HEPS cases
- CD8+ CTL responses in the HEPS population are associated with HIV-1 specific CD4+ T-cell responses, assayed by proliferation assays, IL-2 secretion, and ELISPOT, and the authors consider the possibility that HIV-1-specific T-help responses improve the "quality" of the CD8+ response in HEPS individuals relative to HIV-1 infected individuals, who tend to have a poor HIV-1-specific T-help response
- HIV-1 specific CD8+ CTL responses in HIV-1 infected individuals show reduced levels of perforin, and the T-cells may not mature properly, and although similar studies have not been conducted in HEPS individuals this is considered as a possible difference in the CTL immune response in HEPS and HIV-1 infected people

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Pol( )	Pol( )	HIV-1 infection	human(A*0201, Cw*08)	[Shacklett (2000)]

- HIV-1 specific, MHC class I-restricted CTL killing was detected in duodenal and rectal gut associated lymphoid tissue (GALT) sites from three infected individuals – the distribution of class I restricted CTL was different in the peripheral blood samples and GALT samples

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Pol( )	Pol( )	Vaccine	murine(H-2^d)	[Huang (2001)]

Vaccine: *Vector/type:* DNA *Strain:* gag HxB2, pol NL43 *HIV component:* Gag, Pol

- Mice were immunized with four humanized DNA constructs: GagPol, that would form a pseudoparticle carrying Gag and Pol, Gag, Pol or a GagPol fusion construct
- The GagPol pseudoparticle, Gag and GagPol fusion construct all elicited strong anti-Gag CTL, but only the GagPol fusion construct elicited strong anti-Pol CTL
